



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2022-P-2229]

Determination That Hydrochlorothiazide Oral Solution, 50 Milligrams Per 5 Milliliters, Was Not Withdrawn From Sale for Reasons of Safety or Effectiveness

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA, Agency, or we) has determined that hydrochlorothiazide oral solution, 50 milligrams (mg)/5 milliliters (mL), was not withdrawn from sale for reasons of safety or effectiveness. This determination means that FDA will not begin procedures to withdraw approval of abbreviated new drug applications (ANDAs) that refer to this drug product, and it will allow FDA to continue to approve ANDAs that refer to the product as long as they meet relevant legal and regulatory requirements.

FOR FURTHER INFORMATION CONTACT: Alaina Kupperman, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6215, Silver Spring, MD 20993-0002, 301-796-2395, Alaina.Kupperman@fda.hhs.gov.

SUPPLEMENTARY INFORMATION: Section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(j)) allows the submission of an ANDA to market a generic version of a previously approved drug product. To obtain approval, the ANDA applicant must show, among other things, that the generic drug product: (1) has the same active ingredient(s), dosage form, route of administration, strength, conditions of use, and (with certain exceptions) labeling as the listed drug, which is a version of the drug that was previously approved, and (2) is bioequivalent to the listed drug. ANDA applicants do not have to repeat the extensive clinical testing otherwise necessary to gain approval of a new drug application (NDA).

Section 505(j)(7) of the FD&C Act requires FDA to publish a list of all approved drugs.

FDA publishes this list as part of the “Approved Drug Products With Therapeutic Equivalence Evaluations,” which is known generally as the “Orange Book.” Under FDA regulations, drugs are removed from the list if the Agency withdraws or suspends approval of the drug’s NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (21 CFR 314.162).

A person may petition the Agency to determine, or the Agency may determine on its own initiative, whether a listed drug was withdrawn from sale for reasons of safety or effectiveness. This determination may be made at any time after the drug has been withdrawn from sale, but must be made prior to approving an ANDA that refers to the listed drug (§ 314.161 (21 CFR 314.161)). FDA may not approve an ANDA that does not refer to a listed drug.

Hydrochlorothiazide oral solution, 50 mg/5 mL, is the subject of ANDA 088587, held by Roxane Laboratories Inc., and initially approved on July 2, 1984. Hydrochlorothiazide is indicated for: (1) adjunctive therapy in edema associated with congestive heart failure, hepatic cirrhosis, and corticosteroid and estrogen therapy; (2) edema due to various forms of renal dysfunction such as nephrotic syndrome, acute glomerulonephritis, and chronic renal failure; and (3) the management of hypertension either as the sole therapeutic agent or to enhance the effectiveness of other antihypertensive drugs in the more severe form of hypertension.

In a letter dated August 4, 2008, Roxane Laboratories Inc. requested withdrawal of ANDA 088587 for hydrochlorothiazide oral solution. In the *Federal Register* issue of July 21, 2010 (75 FR 42455), FDA announced that it was withdrawing approval of ANDA 088587, effective August 20, 2010.

Hyman, Phelps & McNamara, P.C. submitted a citizen petition dated September 13, 2022 (Docket No. FDA-2022-P-2229), under 21 CFR 10.30, requesting that the Agency determine whether hydrochlorothiazide oral solution, 50 mg/5 mL, was withdrawn from sale for reasons of safety or effectiveness.

After considering the citizen petition and reviewing Agency records and based on the

information we have at this time, FDA has determined under § 314.161 that hydrochlorothiazide oral solution, 50 mg/5 mL, was not withdrawn for reasons of safety or effectiveness. The petitioner has identified no data or other information suggesting that this product was withdrawn for reasons of safety or effectiveness. We have carefully reviewed our files for records concerning the withdrawal of hydrochlorothiazide oral solution, 50 mg/5 mL, from sale. We have also independently evaluated relevant literature and data for possible postmarketing adverse events. We have reviewed the available evidence and determined that this drug product was not withdrawn from sale for reasons of safety or effectiveness.

Accordingly, the Agency will continue to list hydrochlorothiazide oral solution, 50 mg/5 mL, in the “Discontinued Drug Product List” section of the Orange Book. The “Discontinued Drug Product List” delineates, among other items, drug products that have been discontinued from marketing for reasons other than safety or effectiveness. ANDAs that refer to this drug product may be approved by the Agency as long as they meet all other legal and regulatory requirements for the approval of ANDAs. If FDA determines that labeling for this drug product should be revised to meet current standards, the Agency will advise ANDA applicants to submit such labeling.

Dated: May 8, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

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